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Broad Concepts in Management of Systemic Lupus Erythematosus

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Abstract

Systemic lupus erythematosus is a multisystem autoimmune disease with protean manifestation. Although commonly seen in young women, it can affect men as well as elderly patients. Approach to treatment is multidisciplinary, involves defining the extent of organ involvement, and distinguishing between active manifestations and damage. The mainstay of therapy is judicious use of immunosuppressive medications. Long-term follow-up to address morbidity arising from treatment complications, disease damage, and increased cardiovascular risk is essential.

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Systemic lupus erythematosus (SLE) is a complex systemic autoimmune disease capable of affecting any organ system. Systemic lupus erythematosus is rare, with an incidence of 2.2 to 5.6 cases per 100,000 person-years and a prevalence of 24 to 207 cases per 100,000 person-years, and it is more common in women.[1] It presents earlier and in a more severe form in African Americans, Hispanics, Native Americans, and Asians. The diagnosis of SLE should be suspected in any patient with multiorgan symptoms, and after exclusion of infectious and other causes. The 1997 American College of Rheumatology (ACR) classification criteria can be helpful for diagnosis if 4 of 11 criteria are present; the sensitivity of these is 86% and specificity is 93%.[2] The criticism of ACR criteria is that they place emphasis on mucocutaneous manifestations and do not take into account important neurologic manifestations or isolated lupus nephritis. Furthermore, disease manifestations may accrue over time, making it difficult to make a diagnosis early. To address some of these deficiencies, the Systemic Lupus International Collaborating Clinics classification criteria[2] were proposed. A diagnosis of lupus can be made if patients meet 4 or more criteria, with at least 1 clinical and 1 laboratory criteria. Patients with biopsy-proven lupus nephritis with either positive antinuclear or anti-double stranded deoxyribonucleic acid (dsDNA) antibodies can now be classified as having lupus nephritis, which was not possible with the ACR criteria. The sensitivity of Systemic Lupus International Collaborating Clinics criteria is 94% and specificity 92%.

TREAT-TO-TARGET STRATEGY FOR SLE

A group of international experts proposed a "treat-to-target" strategy for lupus. Such a concept is already effective for the management of diabetes and hypertension, in which treatment is tailored to a goal level of glycosylated hemoglobin or target blood pressure, respectively. The international task force[3] put forth 4 overarching principles and 11 recommendations for management on the basis of extensive literature review. Broad goals include achieving remission or low disease activity, preventing flares, minimizing the use of corticosteroids, not treating patients who are serologically active (high anti—double-stranded DNA and hypocomplementemia) but clinically quiescent and addressing factors affecting health-related quality of life such as depression and pain. Early recognition of lupus nephritis and maintaining immunosuppressive therapy for at least 3 years is recommended. Hydroxychloroquine (HCQ) therapy is recommended for all patients with lupus because of its substantial benefits as discussed below.

There are, however, challenges in implementing such a strategy, including lack of a unified definition of remission and a paucity of effective immunosuppressive agents. Clinical heterogeneity of lupus makes a single disease activity assessment instrument difficult, and many available instruments are

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cumbersome to use in clinical practice. Nevertheless, the treat-to-target strategy is a promising concept. Many organizations[4-8] such as the ACR and European League against Rheumatism have published guidelines for the evaluation and management of patients with SLE and of lupus nephritis.

TREATMENT PRINCIPLES

Key Points

- Treatment decisions are often based on the type and severity of organ involvement.
- There is a paucity of clinical trials and evidence-based recommendations for the treatment of many of the lupus manifestations as well as doses of corticosteroids used.
- Distinction should be made between symptoms manifesting from active disease vs disease-related damage.
- Management of comorbidities, attention to bone health, increased cardiovascular risk, and immunization status should be part of general medical care.
- Active discussion about contraception and preconception planning should be undertaken with patients of childbearing potential.

The treatment approach can be summarized as follows.

General Medical Care

Patients with SLE are at an increased risk of several comorbidities secondary to active disease, damage, or treatment-related complications. The risk of cerebrovascular accidents and ischemic heart disease is increased 2.3-fold in patients with SLE.[9] We have reported a 2- to 3-fold increased risk of cerebrovascular accident and peripheral arterial disease in patients with cutaneous lupus as well.[9] There is an increased risk of infections, osteoporosis, and malignant tumors, especially non–Hodgkin lymphoma, lung, liver, vulvar/vaginal, and thyroid malignancies. Attention should be paid to immunization status, diet, physical activity, and management of fibromyalgia and fatigue. It is critical to take a look at the medication list to identify drugs that can either induce lupus or aggravate lupus skin rashes. The drugs we have commonly noted in our medical practice inducing systemic lupus are minocycline, nitrofurantoin, hydralazine, interferons, and tumor necrosis factor inhibitors. (For a comprehensive review of drug-induced systemic and cutaneous lupus, please refer to Chang and Gershwin.[10])

Table 1 summarizes general medical issues relevant to primary care in these patients.

Contraception

Many patients with lupus are young women taking teratogenic medications, and avoidance of pregnancy during active disease is desirable. The main concerns with hormonal methods of contraception are disease flares and risk of thromboembolism. Two large trials[17,18] have compared various methods of hormonal contraception in patients with SLE. Petri and coworkers conducted a double-blind, randomized, noninferiority trial comparing a triphasic combined oral contraceptive (COC) with a placebo in 183 women. The risk of total flares was not different between the groups. The trial by Sánchez-Guerrero et al compared a COC with a progestin-only pill and copper-containing intrauterine device. The disease activity remained stable and was comparable among the 3 groups. Thrombotic events were seen in 4 patients, 2 in each hormonal group; all patients had low-titer antiphospholipid antibodies. Severe infections were seen in 3 patients in the COC group, 2 in the group receiving the progestin-only pill, and 5 (including 2 cases of meningitis) in the intrauterine device group. Both trials excluded patients with severe disease, smokers, history of thrombosis, history of gynecologic cancers, myocardial infarction, and liver disease. Patients with positive antiphospholipid antibodies and lupus anticoagulant were excluded in the trial by Petri and coworkers but not by Sánchez-Guerrero et al. Barrier methods of contraception, hormonal intrauterine device, injectable progestin are other options.

Supportive Therapy

Patients with lupus are photosensitive, and UV light is associated with flares. It is important for all patients to practice sun protection methods and avoid peak UV-B hours from 10 AM to 4 PM. Sunscreens blocking both UV-A and UV-B with a sun protection factor of 50 or more should be applied liberally and at least 20 minutes before sun exposure. Wide-brimmed